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August 15, 1961

RECENT RESEARCH OF PROFESSOR BOBRAŃSKI AND COWORKERS

I

An interesting part of Bobrański's research has been the transformation of 5,5-diallylbarbituric acid into 5-allyl-5-(β-hydroxypropyl)-barbituric acid (I). With this operation, the hypnotic activity was almost eliminated while a sort of long-lasting tranquilizing effect remained (in man, hardly in animals).[4,5,6,7]

The modification of pharmacodynamic activity realized by chemical means has been considered to be the consequence of the introduction of the hydroxy group into the molecule of diallylbarbituric acid. In order to obtain additional data illustrating the pharmacodynamic role of the hydroxy group in compound I, three esters of it were now prepared and their activities determined: the 3,4,5-trimethoxy benzoic ester, the p-nitrobenzoic ester, and the p-aminobenzoic ester. They showed, however, no distinct pharmacological activities at all. This seems to agree with the theorem that the hydroxy group is necessary to obtain the type of activity shown by I.[8]

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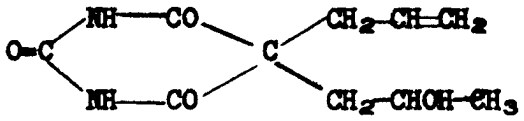


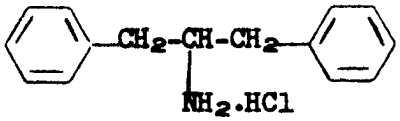
(I)

The 3,4,5-trimethoxybenzoic ester of I melts at 201-201.5°C; the p-nitrobenzoic ester of I has a mp of 215-217°C; the p-aminobenzoic ester of I melts at 183°C.

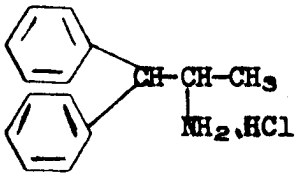
III

Hano and Wojewódski (Dept. of Pharmac., Med. Acad., Wrocław) studied the pharmacological action of three polyphenyl derivatives of aminopropane:[9]

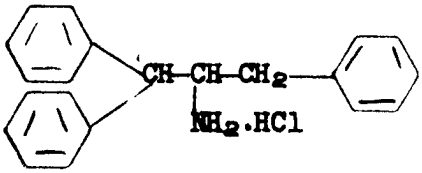
1,3-diphenyl-2-amino-propane (B_{10}) (II)
1,1-diphenyl-2-amino-propane (B_{11}) (III)
1,1,3-triphenyl-2-amino-propane (B_{12}) (IV)



II



III



IV

Two of these substances (compounds B_{10} and B_{11}) or II and III, have been pharmacologically tested before in part while compound B_{12} or III was first synthesized and tested by Bobrański and Jacóbiec (in press, 1961).

All three compounds are more toxic than 'Benzedrine'-SK&F (LD_{50} of 'Benzedrine = 200 mg,kg., LD_{50} of B_{10} or II is 160 mg,kg.; LD_{50} of B_{11} or III is 64 mg,kg.; LD_{50} of B_{12} or IV is 12 mg./kg., animal species and route of administration unrevealed in English abstract at our disposal).[9]

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All three compounds exert a stimulating action on the CNS; they stimulate greatly the respiratory rate, increase the spontaneous or reflex sensibility of animals, cause violent convulsions, and suppress the depressant action of morphine on the respiratory center. Their influence on circulation in toto is analogous to that of 'Benzedrine'-SK&F. Arterial pressure curves show one or two phases, depending on the dose administered; small doses (to 1 mg/kg.) induce occurrance of one phase, enhancing arterial pressure while moderate doses (1-5 mg/kg.) produce a biphasic effect; a short-lasting hypotensive action is followed by a long-lasting decrease in the blood pressure. Atropine suppresses or reduces the hypotensive phase without affecting the hypertensive phase. The opposite is true for regitine.[9]

Cardioplethysmographic studies on the isolated rabbit and frog heart show a deteriorating effect on the heart muscle (bradycardia in spite of atropinization), marked increase in the heart volume and reduction of the systolic-diastolic amplitude.

The Polish workers conclude that the introduction of additional phenyl rings into the phenylisopropylamine molecule produces a marked increase in toxicity while, otherwise, the main properties of the parent compound, 'Benzedrine'-SK&F are not affected.

References

1.

2.

3.

4. Bobrański, B., Jakóbiec, T., and Prelicz, D., Roczniki Chemie 30:175(1956).

5. Kapuściński, W., Gamski, M., and Krudysz, J., Pamiętnik XVI Zjazdu Polskiego Tow. Okulistycznego, Szczecin, 1958, p. 383.

6. Wilimowski, M., Gieldamowski, J., and Kędzierska, L., Archiv. Immunol. i.Terap. Dośw. 7:95(1959).

7. Wilimowski, M., Orzechowska, K., and Kędzierska, L., ibidem. 6:749(1958).

8. Bobrański, B., Gieldanowski, J., Kędzierska, L., and Tumanowicz., A., Archiv. Immunol. i. Terap. Dośw. 9(No.1):1-6(1961).

9. Hano., J., and Wojewodzki, W., Archiv. Immunol. i. Terap. Dośw. 9:7-24(1961).

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